REMARKS

FORMAL MATTERS

Claims 23, 25, 43-46, and 48-55 are pending in this application. Claims 23, 48, and 50-52 have been amended. Support for the amendments to the claims may be found on page 2, line 35 – page 3, line 3; Figure 7A-7I; page 13, line 27 to page 14, line 35 and Figures 6A and 6B (direct repeat sequences appearing in boxes).

WRITTEN DESCRIPTION REJECTION

The Office has maintained the written description rejection of claims 23, 25, 43-46, and 48-52. As previously discussed, the Office appears to believe that the invention as claimed is broadly directed to purified HIV-1 variants that differ genetically in the *gag*, *pol*, and *env* coding regions from three known HIV-1 prototypes (IIIB, BRU, and ARV-2) by the specified amounts (from 9.8-12% in Gag, 5.5-7.7% in Pol, and 20.7-21.7% in Env). Further limitations state that AIDS patient antibodies also bind to the Gag, Pol, or Env polypeptides of the HIV-1 variants and the same polypeptides in HIV-1_{MAL} and that the virus can be detected by stringent hybridization to HIV-1_{MAL} cDNA. The Office states that this encompasses a large genus of genotypically/phenotypically unrelated HIV strains.

As previously, the Office emphasizes that it believes that the specification only describes the molecular cloning and characterization of a single novel HIV-1 isolate, LAV-1_{MAL}. The Office believes that the skilled artisan would not have reasonably concluded that the inventors were in possession of any other HIV-1

variant. The Office states that the specification does not provide information on the isolation, characterization, and nucleotide sequence for any other HIV-1 variants.

Applicants have further amended the claims to provide additional structural limitations. Applicants have amended the claims to recite that the variant viruses hybridize under stringent conditions to the genomic cDNA of HIV-1_{MAL} as shown in Figures 7A-7I or as deposited in the CNCM under No. I-641 **over its entire length**. This amendment would exclude fragments and probes, limiting the claims to a full length virus. The Examiner has objected to the hybridization language as the claims were not so limited.

Applicants have now amended the claims to recite their percentage similarity to the HIV-1_{BRU} sequences (derived from the percentage variation subtracted from 100%), and have also added a new limitation indicating that the sequences contain at least one direct repeat. A pattern of direct repeats has been shown in the LAV_{MAL} viruses, whether an exact repeat or a repeat containing one or two point mutations. These repeats are discussed in the specification on pages 13 and 14, and can be seen in boxed fonts in Figure 6. Figure 6A-1 shows the insertion of one perfect repeat (QQAAAA) in HIV-1_{MAL} Gag. Figure 6A-3 shows the insertion of one perfect repeat (RAEP) and one with two point mutations (DAVSQ) in HIV-1_{MAL} ORF F. Finally, Figure 6B-2 shows the insertion of a repeat with one point mutation (AVNGT) in HIV-1_{MAL} Env and Figure 6B-3 shows the insertion of a repeat with a single point mutation (DNS) in HIV-1_{MAL} Env. These mutations are all specific to HIV-1_{MAL} and are clearly not shown in the other strains in Figure 6. Thus, they can

be used to distinguish HIV-1_{MAL} variants from all other HIV-1 strains. Dependent claim 55 recites all of these specific sequences.

Furthermore, the second limitation (the HIV-1 variant virus binds antibodies in AIDS patient sera, said antibodies binding specifically to the virus designated HIV-1_{MAL}) does not, contrary to the Examiner's assertion, encompass a large genus of unrelated HIV strains. The specification, page 35, lines 26-34, recites that variants of HIV-1_{MAL} are limited to retroviruses having distinguishing characteristics, but still having substantially the same immunological or immunogenic properties. The specification continues by stating "A similar rule of equivalency shall apply to the DNAs." See specification, bridging pages 35-36. Finally, the specification states that "RNAs of these [HIV-1_{MAL}] variants . . . are hybridizable to corresponding parts of the cDNA of LAV_{MAL}" and variants with "some deletions or mutations which would not substantially alter their capability of also hybridizing with the retroviral genome of LAV_{MAL} are to be considered as forming obvious equivalents." See specification, pages 3, lines 5-8 and 16-21.

The specification further provides methods for isolating other HIV-1_{MAL} variants, see page 27, lines 9-5, which specifies that "[l]ymphatic fluids and tissues and other non-lymphatic tissues of humans, primates and other mammalian species can also be screened to see if other evolutionary related retroviruses exist. The methods referred to hereinabove can be used, although hybridization and washings would be done under non-stringent conditions." Page 4, lines 8-22, specify a method to screen genomic DNA derived from the tissue of patients with LAV related

symptoms to see if the proviral DNA or RNA is related to LAV_{MAL}. This method is based on Southern blotting of genomic DNA and hybridization with a probe specific to HIV-1_{MAL}. For example, specific probes could be chosen in hypervariable domains of Env proteins from HIV-1_{MAL} and more specifically from the regions of direct repeats as described above. Therefore, the skilled artisan, given the HIV-1_{MAL} strain and the guidance in the application, could easily isolate an HIV-1 strain equivalent to HIV-1_{MAL}.

Lastly, Applicants wish to point out that the Office has granted similar claims in other applications. For example, in U.S. Patent No. 5,567,703, which was filed significantly later than the present application, the claims are directed to HIV-3 retrovirus and its variants that have the same morphological and immunological properties, even though only the HIV-3 strain was isolated and characterized at the time of the filing of the application.

Thus, the claims provide significant structural features and all of the variant viruses have significant structural commonalities as they are now claimed. It is not necessary to have sequenced or even isolated the variant viruses as the class of viruses was envisioned and defined by the inventors in this application.

Therefore, Applicants request that the Office withdraw this rejection and allow the pending claims.

PRIOR ART REJECTION

The Examiner has again rejected the claims as anticipated by or obvious over *Meyers* (1990), as the Examiner alleges that the claims are not entitled to the benefit of the earlier filed U.S. and foreign applications. *Myers* was published after the U.S. and foreign priority dates (U.S. Appln. Ser. No. 07/038,330, filed April 13, 1987, and European Appln. 86401380.0, filed June 23, 1986). Applicants submit that the specification fulfills the written description requirement and, thus, the *Myers* article, published in 1990, cannot be prior art.

CONCLUSION

Applicants request reconsideration of the claimed invention and early action by the Examiner on the patentability of the claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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